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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/811,367	03/16/2001	Nobuaki Takahashi	021286/027 8719	6403

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EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	14

DATE MAILED: 09/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/811,367	Applicant(s) TAKAHASHI ET AL.	
	Examiner " Neon" Phuong Huynh	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/30/00; 6/25/02* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-61* is/are pending in the application.

4a) Of the above claim(s) *1-38,41-44 and 57-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-40 and 45-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 1-61 are pending.

2. Applicant's election without traverse of Group IV, claims 39-40 and 45-56, drawn to a method for inhibiting an NK or T cell expressed cell surface MAFA binding to a ligand on target cell using an anti-MAFA antibody, filed 6/25/02, is acknowledged.

3. Claims 1-38, 41-44 and 57-61 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

4. Claims 39-40 and 45-56 are being acted upon in this Office Action.

5. The disclosure is objected to because of the following informalities: (1) the "ATCC ___" on page 5 lines 5-9, and page 7, lines 19-23 need to be filled out; (2) The "1 x 106 M-1 or 107 M-1...about 1010 M-1 to 1011 M-1" on page 16, line 3-4 should have been "1 x 10^6 M^{-1} or 10^7 M^{-1}", for example; (3) The "95oC for 5 sec, 55 oC for 30 sec and 72 oC for 2 min" on page 26 line 18 should have been "95°C for 5 sec, 55 °C for 30 sec and 72 °C for 2 min" and (4) "Fc□ RI" on page 32, lines 7-8 should have been "FcεRI". Appropriate action is required.

6. The drawings, filed 3/16/01, are not approved. Please see enclosed PTO 948, Notice of Draftsperson's Patent Drawing Review. Appropriate action is required.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 39-40 and 45-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a method for inhibiting an NK or T cell expressed cell surface Mast Cell Function Associated Antigen (MAFA) binding to a ligand on a target cell comprising the following steps (a) providing a soluble agent that prevents the binding of the NK or the T cell expressed cell surface MAFA to its target cell ligand wherein the soluble agent is an

anti-MAFA antibody; and (b) contacting the anti-MAFA antibody to the NK or the target cell in an amount sufficient to inhibit cell surface MAFA binding to the ligand on the target cell, (2) the method mentioned above wherein the contacting is in vitro or ex vivo, (3) the method mentioned above wherein the target cell is a tumor cell, (4) the method mentioned above wherein inhibiting the NK or the T cell expressed cell surface MAFA binding to the ligand on the target cell prevents or inhibits the NK or T cells expressed cell surface MAFA from generating an inhibitory signal to the NK or the T cell, (5) the method mentioned above wherein the method preventing or inhibiting the NK or T cell expressed cell surface MAFA from generating cytolytic activity of NK or T cell, **does not** reasonably provide enablement for (1) a method for inhibiting an NK or a T cell expressed cell surface MAFA binding to a ligand on a target cell comprising the following steps (a) providing *any* "soluble agent" that prevents the binding of the NK or the T cell expressed cell surface MAFA to its target cell ligand; and (b) contacting *any* "soluble agent" to the NK or the T cell or the target cell in an amount sufficient to inhibit cell surface MAFA binding to the ligand on the target cell, (2) a method for inhibiting an NK or a T cell expressed cell surface MAFA binding to a ligand on a target cell comprising the following steps (a) providing *any* "soluble agent" that prevents the binding of the NK or the T cell expressed cell surface MAFA to its target cell ligand; and (b) contacting *any* "soluble agent" to the NK or the T cell or the target cell in an amount sufficient to inhibit cell surface MAFA binding to the ligand on the target cell wherein the "soluble agent" that prevents the binding of the NK or the T cell expressed cell surface MAFA to its target cell ligand is *any* composition comprising *any* "subsequence of *any* anti-MAFA antibody", wherein the subsequence comprises an antigen binding site, that binds to the cell surface MAFA, (3) a method for inhibiting an NK or a T cell expressed cell surface MAFA binding to a ligand on a target cell comprising the following steps (a) providing *any* "soluble agent" that prevents the binding of the NK or the T cell expressed cell surface MAFA to its target cell ligand; and (b) contacting *any* "soluble agent" to the NK or the T cell or the target cell in an amount sufficient to inhibit cell surface MAFA binding to the ligand on the target cell wherein the contacting is in vitro or ex vivo, (4) a method for inhibiting an NK or a T cell expressed cell surface MAFA binding to a ligand on a target cell comprising the following steps (a) providing *any* "soluble agent" that prevents the binding of the NK or the T cell expressed cell surface MAFA to its target cell ligand; and (b) contacting *any* soluble agent to the NK or the T cell or the target cell in an amount sufficient to inhibit cell surface MAFA binding to the ligand on the target cell wherein the contacting is in vivo, (5) a method for

inhibiting an NK or a T cell expressed cell surface MAFA binding to a ligand on a target cell comprising the following steps (a) providing *any* "soluble agent" that prevents the binding of the NK or the T cell expressed cell surface MAFA to its target cell ligand; and (b) contacting *any* "soluble agent" to the NK or the T cell or the target cell in an amount sufficient to inhibit cell surface MAFA binding to the ligand on the target cell wherein the contacting is in vivo wherein the in vivo contacting comprises administering *any* "soluble agent" to a subject, (6) the said method wherein the subject is *any* mammal, or human, (7) a method for inhibiting an NK or a T cell expressed cell surface MAFA binding to a ligand on a target cell comprising the following steps (a) providing *any* "soluble agent" that prevents the binding of the NK or the T cell expressed cell surface MAFA to its target cell ligand; and (b) contacting *any* "soluble agent" to the NK or the T cell or the target cell in an amount sufficient to inhibit cell surface MAFA binding to the ligand on the target cell wherein the target cell is a tumor cell, (8) a method for inhibiting an NK or a T cell expressed cell surface MAFA binding to a ligand on a target cell comprising the following steps (a) providing *any* "soluble agent" that prevents the binding of the NK or the T cell expressed cell surface MAFA to its target cell ligand; and (b) contacting *any* "soluble agent" to the NK or the T cell or the target cell in an amount sufficient to inhibit cell surface MAFA binding to the ligand on the target cell wherein inhibiting the NK or the T cell expressed cell surface MAFA binding to the ligand on the target cell prevents or inhibits the NK or T cell-expressed cell surface MAFA from generating an inhibitory signal to the NK or the T cell, (9) the method for inhibiting an NK or a T cell expressed cell surface MAFA binding to a ligand on a target cell comprising the following steps (a) providing *any* "soluble agent" that prevents the binding of the NK or the T cell expressed cell surface MAFA to its target cell ligand; and (b) contacting *any* "soluble agent" to the NK or the T cell or the target cell in an amount sufficient to inhibit cell surface MAFA binding to the ligand on the target cell wherein inhibiting the NK or the T cell expressed cell surface MAFA binding to the ligand on the target cell prevents or inhibits the NK or T cell-expressed cell surface MAFA from generating an inhibitory signal to the NK or the T cell wherein preventing or inhibiting the NK or T cell expressed cell surface MAFA from generating an inhibitory signal to the NK or the T cell stimulates any activity of the NK or the T cell, (10) the said method wherein the stimulated NK cell or T cell activity is an increase in NK cell or T cell mediated cell killing or tumor cell killing, (11) the said method wherein the stimulated NK cell or T cell activity is an increase in T killer cell (CTL) activity or *any* cytokine secretion by the T cell, (12) the said method wherein the stimulated NK cell or T

cell activity is an increase in T killer (CTL) activity against virally infected cell for treating *any* disease such as tumor or viral disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a recombinant soluble murine MAFA for making monoclonal antibodies, and a method for inhibiting NK or T cell expressed cell surface MAFA binding to a ligand on a target cell using MAFA specific monoclonal antibody selected from the group consisting of 1F10 and 7B5 or the F(ab')2 binding fragment of said antibody in vitro or ex vivo. The said monoclonal antibody **inhibits** the cytotoxic activity of NK cells or T cells (page 29, and 31). The specification further discloses a method for enhancing the cytotoxic activity of NK cell using recombinant soluble MAFA (Fig 2, page 30) and this cytotoxic or cytolytic activity of NK cell can be inhibit by anti-MAFA antibody mentioned above (See page 31).

The specification does not teach how to make and use a method for inhibiting any NK or T cell expressed cell surface MAFA binding to *any* ligand on a target cell using (1) *any* soluble agent, (2) *any* composition comprising *any* "subsequence of *any* anti-MAFA antibody" wherein the subsequence "comprises" an antigen binding site that bind to the cell surface MAFA. The term "soluble agent" has no structure and function. Since the "agent" has no structure (amino acid sequence, SEQ ID), even one of skilled in the art could not make and use the claimed invention. Given the indefinite number of agent, it is unpredictable which undisclosed "soluble agent" would have the same structure and function as the claimed MAFA specific antibody, in turn, would be effective for a method for inhibiting any NK or T cell expressed cell surface MAFA binding to the ligand on a target cell, and thereby preventing or stimulating NK or T cell cytolytic activity in vitro, much less in vivo for treating tumor or virally infection.

With regard to *any* subsequence of any MAFA antibody, the specification discloses only two specific MAFA antibodies such as 1F10 and 7B5 or the F(ab')2 binding fragment of said antibody that can inhibit NK and CTL activity. There is insufficient guidance and in vivo working examples demonstrating *any* "subsequence of *any* MAFA antibody" can inhibit or enhance NK or T cell killing of tumor cell or viral infected cell. Even if the soluble antigen is limited to the specific anti-MAFA antibody, there is no working example demonstrating that any of the claimed anti-MAFA antibodies or any subsequence of the claimed antibody can "**increase**" NK cell or T cell mediated killing of tumor cells or virally infected cell in vitro, let alone in vivo.

Kuby *et al* teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide. Without the specific amino acid residues, it is unpredictable to determine which undisclosed subsequence of *any* anti-MAFA antibody wherein the subsequence "comprises" an antigen binding site would have the same antibody specificity as an antibody generated from the full-length polypeptide. Further, the term "comprises" is open-ended. It expands the "subsequence" to include additional amino acids at either or both ends of an antigen-binding site. There is no guidance in the specification as to what type and number of amino acids within the amino acid sequence (polypeptide) of any anti-MAFA antibody binding region can be added and whether after addition of amino acids would retain the structure and function. There are no working examples of *any* subsequence of *any* anti-MAFA antibody can prevent the binding of the NK or the T cell to its ligand, much less increase or prevent NK or T cell cytolytic activity.

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Abaza *et al* teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular). Given the indefinite number of undisclosed "soluble agent", antibody, and subsequence "comprises" an antigen binding site of any antibody, it is unpredictable which undisclosed "soluble agent", antibody, and subsequence "comprises" an antigen binding site of

any antibody would be effective for a method for inhibiting NK or T cell expressed cell surface MAFA from generating an inhibitory signal to the NK or the T cell, in turn to stimulate NK and T cell activity in vitro or in vivo. Since the amino acid sequence and specificity of *any* anti-MAFA antibody and subsequence are not enabled, it follows that the method of making and the method for inhibiting any NK or T cell expressed cell surface MAFA binding to a ligand on a target cell and thereby inhibiting the NK or T cell cytolytic activity against tumor or viral infected cells in vitro and in vivo is not enable. It also follows that any soluble agents such as any anti-MAFA, any subsequence of any anti-MAFA for a method for inhibiting the NK or T cell expressed cell surface MAFA from generating any inhibitory signal to NK or T cell to stimulates NK or T cell activity such as increase in NK cell or CTL killing of any tumor cell or viral infected cell in vitro or in vivo are not enable.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

9. Claims 39-40 and 45-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of a method for inhibiting any NK or T cell expressed cell surface MAFA binding to *any* ligand on a target cell using (1) *any* "soluble agent" and (2) *any* composition comprising *any* "subsequence" of *any* anti-MAFA antibody wherein the subsequence "comprises" an antigen binding site that bind to the cell surface MAFA in vitro *or* in vivo.

The specification discloses only a recombinant soluble murine MAFA for making monoclonal antibodies, and a method for inhibiting NK or T cell expressed cell surface MAFA

binding to a ligand on a target cell using MAFA specific monoclonal antibody selected from the group consisting of 1F10 and 7B5 or the F(ab')2 binding fragment of said antibody in vitro or ex vivo. The said monoclonal **antibody inhibits** the cytotoxic activity of NK cells or T cells (page 29, and 31). The specification further discloses a method for enhancing the cytotoxic activity of NK cell using recombinant soluble MAFA (Fig 2, page 30) and this cytotoxic or cytolytic activity of NK cell can be inhibit by anti-MAFA antibody mentioned above (See page 31).

With the exception of the anti-MAFA antibodies mentioned above, there is insufficient written description about the structure associated with function of (1) *any* "soluble agent" and (2) *any* subsequence of *any* anti-MAFA antibody wherein the subsequence "comprises" an antigen binding site that bind to the cell surface MAFA in vitro or in vivo as a method for inhibiting any NK or T cell expressed cell surface MAFA binding to *any* ligand on a target cell. Further, the term "comprising" is open-ended. It expands the "subsequence" of *any* antigen binding site of *any* anti-MAFA antibody to include additional amino acids at either or both ends. Given the lack of a written description of *any* additional representative species of "soluble agent", and "composition of comprising *any* subsequence of *any* anti-MAFA antibody wherein the subsequence "comprises" an antigen binding site, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

11. Claims 40, 52 and 55-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "a composition comprising a subsequence of an anti-MAFA antibody" in claim 40 is indefinite and ambiguous because the claimed as written recites a compound and not a composition.

The recitation of " the T cell stimulates an activity of the NK or the T cell" in claim 52 is ambiguous and indefinite because one of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention. The term "stimulates" appears to contradict the "inhibitory signal". Further, it is not clear which "activity" of NK or T cell is being claimed.

The recitation of "cytokine secretion" in claim 55 is ambiguous and indefinite because it is not clear which *cytokine* is being secreted by the T cell in the claimed method since more than one cytokines are secreted by T cells. One of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 39-40 and 46-56 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/54209 publication (December 1998, PTO 1449).

The WO 98/54209 publication teaches a method for preventing T cell activation in human (mammal) which could lead to the prevention of tumor growth by administering a pharmaceutical composition comprising soluble agent such as antibody to human MAFA or fragment thereof (the binding fragment is a subsequence of an anti-MAFA antibody) (See Abstract, claims 1-11, 24, and 26 of WO 98/54209 publication, in particular). The reference soluble agent such as antibody and binding fragment are specific for the C terminal extracellular domain (Claims 8 and 13of WO 98/54209 publication, in particular) which inherently inhibit T cell expressed cell surface MAFA from binding to a ligand on a target cell since it prevent T cell activation (See abstract, in particular). The WO 98/54209 publication teaches MAFA is a C type lectins found on NK cells (See page 2, second paragraph, in particular) and the MAFA function as an "off" switch which generates inhibitory signal to cells such as mast cells, NK cells and T cells (See page 5, third paragraph, in particular). Claims 53-54 are included in this rejection because the reference method use soluble agent to treat tumor, which inherently increases T cell killing activity such as tumor cell. Claim 56 is included in this rejection because the mechanism of T cell mediated killing of tumor and virally infected cells is the same. Thus, the reference teachings anticipate the claimed invention.

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/54209 publication (December 1998, PTO 1449).

The teachings of the WO 98/54209 publication have been discussed supra.

The claimed invention as recited in claim 45 differs from the reference only by the recitation that the method of inhibiting an NK or T cell expressed cell surface MAFA binding to a ligand on a target cell wherein the contacting soluble agent to its target cell ligand is in vitro. Since the WO 98/54209 publication teaches contacting the reference agent in vivo could inhibit NK cell or T cell surface binding to a ligand on target cell in vivo, it would have been obvious that the same inhibition would applied in vitro. Therefore, it is an obvious variation of the reference teaching of contacting the reference agent in vitro.

17. Claims 39, 51-53, 55 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/54209 publication (December 1998, PTO 1449) in view of Blaser *et al* (J Immunol 161: 6451-54, 1998; PTO 1449) or Hanke *et al* (Eur J Immunol 28: 4409-4417, 1998; PTO 1449).

The teachings of the WO 98/54209 publication have been discussed supra.

The claimed invention as recited in claim 53 differs from the reference only by the recitation that the method wherein the stimulated NK cell or T cell activity is an increase in NK cell or T cell-mediated killing.

The claimed invention as recited in claim 56 differs from the reference only that the stimulated T cell activity is an increase in T killer cell (CTL) against virally infected cells.

Blaser *et al* teach MAFA is a member of C type lectin receptor that function as inhibitory receptor on NK cells and viral infected (activated) CD8 T cytotoxic cells (See page 6451, column 2, in particular). Blaser *et al* teach activated T cell (viral infection) increases MAFA expression and T cell-mediated killing (See Fig 3, in particular).

Hanke *et al* teach soluble agent such as 2F1 antigen, which is a mouse homolog of rat MAFA receptor that binds to MAFA on NK cells and may modulate immunological response (See Abstract, page 4409, column 2, page 4411, column 2, Fig 4 and 5in particular). Hanke *et al* teach MAFA expression is associated with increase NK cell killing (LAK cells) (See page 4412, column 2, first full paragraph, in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to include cell such as NK cells as taught by Blaser *et al* and Hanke *et al* or CTL as taught by Blaser *et al* for a method for inhibiting NK or T cell expressed cell surface MAFA binding to a ligand on a target cell to stimulate NK and T cell mediated cell killing against virally infected cells as taught by the WO 98/54209 publication, Blaser *et al* and Hanke *et al*. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Blaser *et al* teach MAFA is a member of C type lectin receptor that function as inhibitory receptor on NK cells and T cells and virally activated (infected) T cells increase MAFA expression (See page 6451, column 2, in particular). Hanke *et al* teach soluble agent such as 2F1 antigen, which is a mouse homolog of rat MAFA receptor that binds to MAFA on NK cells and may modulate immunological response such as NK cell killing activity since MAFA expression increases in NK cell (See page 4412, column 2, first full paragraph, in particular).

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

20. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
September 30, 2002

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600